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ACUTE 15-MINUTE, NOSE-ONLY INHALATION EXPOSURES OF HALON 1301 TO MALE AND FEMALE SPRAGUE-DAWLEY RATS

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TECHNICAL REVIEW AND APPROVAL

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The experiments reported herein were conducted according to the "Guide for the Care and Use of Laboratory Animals," Institute of Laboratory Animal Resources, National Research Council.

This report has been reviewed by the Office of Public Affairs (PA) and is releasable to the National Technical Information Service (NTIS). At NTIS, it will be available to the general public, including foreign nations.

This technical report has been reviewed and is approved for publication.

FOR THE COMMANDER

TERRY A. CHILDRESS, Lt Col, USAF, BSC
Director, Toxicology Division
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To make comparisons of short-term lethality on trifluoroiodomethane (CF_3I) and Halon 1301, 15-minute, nose-only inhalation exposures were performed at 30, 50, and 80% Halon 1301. Slight tremors and ataxia were noted following 50 and 80% Halon 1301 exposures. All animals survived and gross examination at 14 days postexposure indicated normal findings. The lack of mortality at these concentrations indicate that Halon 1301 is less potent than CF_3I.

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PREFACE

This is one of a series of technical reports describing results of the experimental laboratory programs conducted at the Toxic Hazards Research Unit, ManTech Enviromental Technology, Inc. This document serves as a final report on the acute nose-only inhalation toxicity of Halon 1301. The research described in this report began in April 1994 and was completed in May 1994 under U.S. Air Force Contract No. F33615-90-C-0532 (Study No. F25). Lt Col Terry A. Childress served as Contract Technical Monitor for the U.S. Air Force, Harry G. Armstrong Laboratory, Toxicology Division.

The animals used in this study were handled in accordance with the principles stated in the *Guide for the Care and Use of Laboratory Animals*, prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animals Resources, National Research Council, Department of Health and Human Resources, National Institutes of Health Publication #86-23, 1985, and the Animal Welfare Act of 1966, as amended.

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ABBREVIATIONS

(Study F25)

CF_3I	Trifluoroiodomethane
h	Hour
LC_{50}	Median lethal concentration
N	Number
N_2	Nitrogen
ppm	Parts per million
psi	Pounds per square inch

SECTION 1
INTRODUCTION

The flooding agent for extinguishing in-flight aircraft and electronic equipment fires currently being used by the Air Force is Halon 1301 (bromotrifluoromethane). Halon 1301 is a fully halogenated hydrocarbon of relatively low toxicity. However, environmental concerns about the contribution of Halons to depletion of stratospheric ozone and global warming has resulted in an attempt to find adequate replacements. A compound being considered, because it is believed to have less ozone-depleting activity, is trifluoroiodomethane (CF_3I). Extensive testing is being performed on CF_3I including short-term acute toxicity evaluations. Kinkead et al. (1994) reported nose-only inhalation exposures of CF_3I to male Fischer 344 rats at concentrations of 0.5 and 1.0% in which all rats survived 4-h exposures. Histopathologic examination of tissues at various time points following exposure indicated normal findings. Fifteen-minute, nose-only inhalation exposures have been performed on CF_3I at concentrations ranging between 13 and 29% (Skaggs et al., 1993; Ledbetter, 1994). A 15-min inhalation median lethal concentration (LC_{50}) for Sprague-Dawley rats has been established at 27% CF_3I.

To make comparisons on short-term lethality of CF_3I and Halon 1301 it was necessary to perform 15-min, nose-only inhalation exposures of Halon 1301 under conditions similar to those used to establish the toxicity of CF_3I. This will provide information necessary to make valid judgements in assessing the comparative risks of the two fire extinguishants.

SECTION 2
MATERIALS AND METHODS

TEST COMPOUND

The Halon 1301, supplied from the Air Force inventory, is a liquid and was stored in a cylinder under pressure. Pertinent physical and chemical properties follow:

CAS No.	75-63-8
Systematic Name	Bromotrifluoromethane
Molecular Weight	148.91
Empirical Formula	$CBrF_3$
Physical State	Colorless gas
Vapor Density (Air=1)	5.12
Melting Point	-168 °C
Boiling Point	-57.8 °C
Flash Point	Not flammable
Vapor Pressure	205 psi @ 21 °C (Approx. 10,600 mmHg)
Solubility in water	Very slight

TEST ANIMALS

Twenty male and 20 female Sprague-Dawley rats were purchased from Charles River Breeding Laboratories, Raleigh, NC. The rats were 7 weeks of age upon arrival and 9 weeks of age at the time of exposure. All rats were identified by tail tattoo and were subjected to a 2-week quarantine period. Water and feed (Purina Formulab #5008) were available *ad libitum* except during exposure. Animal room temperatures were maintained at 21–25 °C, and the light/dark cycle was set at 12-h intervals. The animals were group housed (two per cage, except during exposure) in clear plastic cages with wood chip bedding (Betta-Chip, Northeastern Products Corp., Warrensburg, NY).

GENERATION AND ANALYSIS OF EXPOSURE ATMOSPHERES

Halon 1301 vapor was generated from a cylinder through a calibrated Matheson rotometer (Matheson Gas Products, Secaucus, NJ). The Halon 1301 vapor was combined with oxygen (20–21% of total flow) and nitrogen (N_2), which was added as required to produce a combined N_2 and Halon 1301 mixture of 79–80%. The Halon 1301 concentration was continuously monitored using a flow-through, 10-cm path cell, with a Miran 1A infrared analyzer (Foxboro, S. Norwalk, CN) at the absorption band of 11.7 μm. Calibration curves were developed using Tedlar sample bags (SKC, Eighty-four, PA).

The flow-through chamber was monitored and the exposure concentration was maintained prior to introducing the test animals. The animals were introduced to the exposure over time. Each rat was removed from the chamber and the port was resealed following 15 min of exposure. Because the animals were introduced to the exposure system over time, the total chamber monitoring time was 20 min. The exposure concentrations were monitored continuously. A digital value was recorded at 5-min intervals and used for concentration calculation. Temperature and humidity within the Cannon chamber were not monitored. Oxygen concentration was monitored using a Hudson Oxygen Monitor (Model #5590, Hudson Electronics Division, Temeculda, CA) calibrated with room air as 21%.

The nose-only chamber was a stainless steel flow-past chamber as described by Cannon et al. (1983). The chamber had 52 ports; 10 were randomly selected for rat exposure. Plexiglas rat restraining tubes that extended radially outward were plugged into the ports. The remaining ports were capped or used for monitoring chamber atmosphere conditions.

EXPOSURE REGIMEN

Each nose-only exposure was for 15 min. The flow-through exposure system was maintained at the target concentration prior to the introduction of the test animals. The containment tubes with animals were attached to the exposure system, one at a time, at 30-s intervals. The animals were withdrawn from the system in a similar manner. The exposure groups consisted of five male and five female rats per concentration level and the rats were maintained 14 days postexposure for evaluation. A total of 15 male and 15 female rats were included in each of three exposures, at target concentrations of 30, 50, and 80% Halon 1301.

TOXICITY ASSESSEMENTS

Records were maintained of body weights and signs of toxicity. Euthanasia was via halothane inhalation overdose. At sacrifice, gross pathology was performed on all rats.

SECTION 3
RESULTS

EXPOSURE SYSTEM ANALYSIS

The specified target concentrations of 30, 50, and 80% Halon 1301 were maintained during the 15-min exposure periods. The exposure mean concentrations were maintained within ±2% of the desired concentrations. Mean concentrations for each exposure, along with the mean high and low concentrations, are provided in Table 1.

TABLE 1. ANALYSIS OF HALON 1301 CONCENTRATION INHALED BY MALE AND FEMALE SPRAGUE-DAWLEY RATS

Target Concentration (%)	30.0	50.0	80.0
Mean Concentration, N=5 (%)	30.2	50.3	81.3
Standard Deviation	0.2	0.1	0.4
Maximum Concentration (%)	30.6	50.4	81.7
Minimum Concentration (%)	30.0	50.2	81.0

INHALATION TOXICITY

There were no deaths resulting from exposure. Female rats exposed at 50% Halon 1301 showed mild tremors and slight incoordination following exposure. Both male and female rats demonstrated mild tremors and slight incoordination following the 80% exposure. The tremors and incoordination dissipated by 10 min postexposure. Mean body weight gains during the 14-day observation period followed a normal pattern for Sprague-Dawley rats (Table 2) based on historical control data.

All rats were examined grossly at the conclusion of the 14-day observation period. No gross lesions that could be attributed to exposure were noted.

TABLE 2. BODY WEIGHTS[a] OF SPRAGUE-DAWLEY RATS EXPOSED FOR 15 MINUTES TO HALON 1301 VIA NOSE-ONLY INHALATION

Halon 1301 Concentration (%)	Day (Pre- and Postexposure)		
	0	7	14
		Males	
80	361.8±19.6	398.6±22.1	436.9±22.7
50	343.2±31.3	368.3±46.9	411.4±60.4
30	323.1±6.1	368.6±6.9	411.5±9.3
		Females	
80	256.7±11.3	270.1±16.5	290.5±16.7
50	232.0±12.5	261.4±7.4	284.0±15.6
30	223.7±18.3	242.2±17.2	263.9±25.2

[a]Mean ± SD (N=5)

SECTION 4
DISCUSSION

Acute (15-min) inhalation of Halon 1301 at concentrations of 30, 50, and 80% (300,000, 500,000, and 800,000 ppm) did not result in mortality to either male or female Sprague-Dawley rats. Signs of toxic stress were limited to slight tremors and slight loss of coordination following exposure to 50 or 80% Halon 1301, which dissipated by 10 min postexposure. Gross examination of tissues at 14 days postexposure indicated normal findings.

The lack of mortality in rats at these exposure concentrations is in agreement with that reported by Chambers and Krackow (1950), Comstock et al. (1950), and MacNamee (1950), in which rats survived exposures to high concentrations of Halon 1301 for 15 min. The lack of mortality in the rats exposed at these concentrations would indicate that Halon 1301 is less potent than CF_3I (15 min LC_{50} of 27%).

SECTION 5

REFERENCES

Cannon, W.C., E.F. Blanton, and K.E. McDonald. 1983. The flow-past chamber: An improved nose-only exposure system for rodents. *Am. Ind. Hyg. Assoc. J.* 44(12):923-933.

Chambers, W.H. and E. H. Krackow. 1950. An investigation of the toxicity of fire extinguishing liquids. Part I. Summary. Medical Division Research Report No. 23, Chemical Corps, Army Chemical Center, MD.

Comstock, C.C., F.P. McGrath, S.B. Goldberg, and L.H. Lawson. 1950. An investigation of the toxicity of proposed fire extinguishing fluids. Part II. The approximate lethal concentration to rats by inhalation of vapors for 15 mins. Medical Division Research Report No. 23, Chemical Corps, Army Chemical Center, MD.

Kinkead, E.R., S.A. Salins, R.E. Wolfe, H.F. Leahy, and J.H. English. 1994. Acute toxicity evaluation of Halon replacement trifluoroiodomethane (CF_3I). AL-TR-1994-____, Armstrong Laboratory, Wright-Patterson Air Force Base, OH.

Ledbetter, A. 1994. Personal communication.

MacNamee, J.K. 1950. An investigation of the toxicity of proposed fire extinguishing fluids. Part III. The pathology in rats produced by inhalation of proposed fire extinguishing fluids. Medical Division Research Report No. 23, Chemical Corps, Army Chemical Center, MD.

Skaggs, S.R., D.S. Dierdorf, and R.E. Tapscott. 1993. Update on iodides as fire extinguishing agents. International CFE and Halon Alternatives Conference, Washington, DC, pp. 800-808.

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